Personnel, Facilities, Environment, Supplies, Cleaning

FDA and the New Paradigm for Tissue Regulation

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NOTE

- These regulations apply to “manufacture” of HCT/Ps, not just to processing. So, must be used, when and where appropriate.
- For example –
  - Environmental controls may be necessary for recovery operations but not for donor screening
  - Personnel training appropriate across the board

Comments: Personnel

- Two comments supported as proposed; however, requirements for organizational structure and documentation of training omitted in final rule
- Comments on need for specific criteria/guidelines for training; requests for clarification on qualifications
  - Response – number of ways to comply; left up to individual establishments

Personnel
§1271.170

- No core GTP requirements
- (a) General. You must have personnel sufficient to ensure compliance with the requirements of this part.
- (b) Competent performance of functions. You must have personnel with the necessary education, experience, and training to ensure competent performance of their assigned functions. Personnel must perform only those activities for which they are qualified and

§1271.170

- c) Training. You must train all personnel, and retrain as necessary, to perform their assigned responsibilities adequately.

Comments: Facilities

- Three comments on limiting to preventing transmission of disease
  - Response – We agreed and added language in this regard
- Clarification of the term “location” (suitable)
  - Response – Examples of unsuitable – on a loading dock or in same building as a slaughterhouse

Comments: Facilities

- Comment on developing and maintaining cleaning procedures for all areas; should not require
  - Response – acknowledge regulation meant to include areas used for manufacture of HCT/Ps to prevent introduction, spread, or transmission of communicable disease; further clarification added; not meant to include all cleaning activities (e.g. vacuuming the lobby).

Comments: Facilities

- Comment opposed to keeping mopping records for 10 years
  - Response – not necessary to keep actual mopping records but documentation that cleaning in accordance with procedures took place (e.g. a task log). Record retention requirement shortened from 10 to 3 years, which allows availability for each inspection cycle.

Facilities
§1271.190

- 1271.190(a) and (b) are core GTP requirements
- (a) General. Any facility used in the manufacture of HCT/Ps must be of suitable size, construction, and location to prevent contamination of HCT/Ps with communicable disease agents and to ensure orderly handling of HCT/Ps without mix-ups. You must maintain

§1271.190

- the facility in a good state of repair. You must provide lighting,

  ventilation, plumbing, drainage, and access to sinks and toilets that are adequate to prevent the introduction, transmission, or spread of communicable disease.

§1271.190

- (b) Facility cleaning and sanitation.
- (1) You must maintain any facility used in the manufacture of HCT/Ps in a clean, sanitary, and orderly manner, to prevent the introduction, transmission, or spread of communicable disease.
- (2) You must dispose of sewage, trash, and other refuse in a timely, safe, and sanitary manner.

§1271.190

- (c) Operations. You must divide a facility used in the manufacture of HCT/Ps into separate or defined areas of adequate size for each operation that takes place in the facility, or you must establish and maintain other control systems to prevent improper labeling, mix-ups, contamination, cross-contamination, and accidental exposure of HCT/Ps to communicable disease agents.

§1271.190

- (d) Procedures and records.
- (1) You must establish and maintain procedures for facility cleaning and sanitation for the purpose of preventing the introduction, transmission, or spread of communicable disease. These procedures must assign responsibility for sanitation and must describe in sufficient detail the cleaning methods to be used and the schedule for cleaning the facility.

§1271.190

- (2) You must document, and maintain records of, all cleaning and sanitation activities performed to prevent contamination of HCT/Ps. You must retain such records 3 years after their creation.

Comments: Environmental Control

- Three comments questioned applicability to eye banking
  - Response – regulation states “where environmental conditions….reasonably be expected to cause…” and “where appropriate.” Based on individual establishment and manufacturing procedures.

Comments: Environmental Control

- Comment on type of organisms to monitor for: should be more specific
  - Response – based on individual establishment. May vary from establishment to establishment; room to room; (I would add: season to season – e.g. mold in humid months). Reference to Guidance for Industry on Aseptic Processing; August 2003 and the USP.

Environmental Control and Monitoring 1271.195

- 1271.195 (a) is a core GTP requirement
- (a) Environmental control. Where environmental conditions could reasonably be expected to cause contamination or cross-contamination of HCT/Ps or equipment, or accidental exposure of HCT/Ps to communicable disease agents, you must adequately control environmental conditions and provide proper conditions for operations. Where appropriate, you must provide for the following control activities or systems:

§ 1271.195

- (1) Temperature and humidity controls;
- (2) Ventilation and air filtration;
- (3) Cleaning and disinfecting of rooms and equipment to ensure aseptic processing operations; and
- (4) Maintenance of equipment used to control conditions necessary for aseptic processing operations.

§ 1271.195

- (c) Environmental monitoring. You must monitor environmental conditions where environmental conditions could reasonably be expected to cause contamination or cross-contamination of HCT/Ps or equipment, or accidental exposure of HCT/Ps to communicable disease agents. Where appropriate, you must provide environmental monitoring for microorganisms.

§ 1271.195

- (d) Records. You must document, and maintain records of, environmental control and monitoring activities.

What about Monitoring?

- Consider designing to provide useful information on normal flora:
  - Establishment of adequate cleaning procedures
  - Measure of effectiveness of cleaning
  - Detection of problems before out-of-control
  - Effectiveness of personnel training in aseptic practices/techniques
- Adjustments based on data

Comments: Equipment

- Comment that regulation to broad; limit to prevention of transmission of disease; allow individual establishments to establish and maintain appropriate procedures.
  - Response – We agreed with comments and provided further clarification in the regulation

Comments: Equipment

- Comment opposing inclusion of “computers” and certain equipment (e.g. slit lamps) as requiring calibration.
  - Response – We agreed. Removed reference to computers and added the phrase “where appropriate” in relation to this requirement.

Comments: Equipment

- Eight comments objected to requirement for maintenance, cleaning, sanitizing, etc. records be kept “at each piece of equipment.”
  - Response – We agreed and revised regulation to allow for having the records readily available for personnel performing these activities and those using the equipment.

Comments: Equipment

- Comment that record requirements be limited to major equipment; “simple instruments” and disposable instruments not be included.
  - Response – We disagreed that simple instruments be exempted but agreed that single-use instruments be exempted if used once and disposed of after use.

Equipment §1271.200

- 1271.200(a) is core GTP requirement
- a) General. To prevent the introduction, transmission, or spread of communicable diseases, equipment used in the manufacture of HCT/Ps must be of appropriate design for its use and must be suitably located and installed to facilitate operations, including cleaning and maintenance. Any automated, mechanical, electronic, or other equipment used for inspection, measuring, or testing in accordance with this part must be capable of producing valid results. You must clean, sanitize, and maintain equipment according to established schedules.

§1271.200

- (b) Procedures and schedules. You must establish and maintain procedures for cleaning, sanitizing, and maintaining equipment to prevent malfunctions, contamination or cross-contamination, accidental exposure of HCT/Ps to communicable disease agents, and other events that could reasonably be expected to result in the introduction, transmission, or spread of communicable diseases.

§1271.200

- c) Calibration of equipment. Where appropriate, you must routinely calibrate according to established procedures and schedules all automated, mechanical, electronic, or other equipment used for inspection, measuring, and testing in accordance with this part.

c)

§1271.200

- (d) Inspections. You must routinely inspect equipment for cleanliness, sanitation, and calibration, and to ensure adherence to applicable equipment maintenance schedules.

§1271.200

- (e) Records. You must document and maintain records of all equipment maintenance, cleaning, sanitizing, calibration, and other activities performed in accordance with this section. You must display records of recent maintenance, cleaning, sanitizing, calibration, and other activities on or near each piece of equipment, or make the records readily available to the individuals responsible for performing these activities and to the personnel using the equipment. You must maintain records of the use of each piece of equipment, including the identification of each HCT/P manufactured with that equipment.

Comment: Supplies and Reagents

- One comment asked for clarification on whether receipt requirements pertained to supplies solely used in recovery
  - Response – No. Requirements pertain to all steps in manufacture. In response to this and other comments, have further clarified to prevention of introduction, transmission, or spread of communicable disease.

Comment: Supplies and Reagents

- Comment asking whether limited to supplies that come in direct contact with the donor or recovered tissue.
  - Response – clarified for all supplies and reagents. Example given: a reagent used in donor testing.

Supplies and Reagents § 1271.210

- 1271.120(a) and (b) are core GTP requirements
- a) Verification. You must not use supplies and reagents until they have been verified to meet specifications designed to prevent circumstances that increase the risk of the introduction, transmission, or spread of communicable diseases. Verification may be accomplished by the establishment that uses the supply or reagent, or by the vendor of the supply or reagent.

What about cleaning?

- 1271.190(b) a core GTP requirement for facility cleaning
- (b) Facility cleaning and sanitation.
- (1) You must maintain any facility used in the manufacture of HCT/Ps in a clean, sanitary, and orderly manner, to prevent the introduction, transmission, or spread of communicable disease.

What about Cleaning?

- 1271.190(d) Procedures and records.
- (1) You must establish and maintain procedures for facility cleaning and sanitation for the purpose of preventing the introduction, transmission, or spread of communicable disease. These procedures must assign responsibility for sanitation and must describe in sufficient detail the cleaning methods to be used and the schedule for cleaning the facility.

What about Cleaning?

- 1271.190(d)(2) You must document, and maintain records of, all cleaning and sanitation activities performed to prevent contamination of HCT/Ps. You must retain

What about cleaning?

- Equipment – 1271.200(a) core GTP requirement
  - "You must clean, sanitize, and maintain equipment according to established schedules."
  - 1271.200(b)-You must establish and maintain procedures for cleaning, sanitizing, and maintaining equipment to prevent malfunctions, contamination or cross-contamination, accidental exposure of HCT/Ps to communicable disease agents, and other events that could reasonably be expected to result in the introduction, transmission, or spread of communicable diseases.

What about Cleaning?

- 1271.200(d) Inspections. You must routinely inspect equipment for cleanliness, sanitation, and calibration, and to ensure adherence to applicable equipment maintenance schedules.

What about Cleaning?

- 1271.200(e) Records. You must document and maintain records of all equipment maintenance, cleaning, sanitizing, calibration, and other activities performed in accordance with this section. You must display records of recent maintenance, cleaning, sanitizing, calibration, and other activities on or near each piece of equipment, or make the records readily available to the individuals responsible for performing these activities and to the personnel using the equipment. You must maintain records of the use of each piece of equipment, including the identification of each HCT/P manufactured with that equipment.

What about Cleaning?

- Regulations do not require validation of cleaning.
- However, thought should be given in establishing these procedures in keeping with what is required – prevention of introduction, spread, or transmission of communicable disease agents.
- Special consideration given to process-related cleaning as process validation/verification is required.

What about Cleaning?

- Problems seen:
  - Reliance on one disinfectant, e.g. Isopropyl Alcohol (IPA); not broad spectrum; proliferation of unaffected microorganisms
  - Use of cleaning agents demonstrated to provide certain disinfecting/sanitizing properties but failure to follow manufacturer's instructions (dilution, contact time).

What about Cleaning?

- Lessons Learned:
  - Consider rotating use of disinfectants/sanitizing agents: take broad spectrum approach
  - Follow the manufacturer's directions – include in relevant procedures and documentation